Convergence of medical science and technology—the Sree Chitra Tirunal Institute

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Fourteen years is less than a generation, and no more than a moment in the history of scientific institutions. That is the period of combined existence of the Sree Chitra Tirunal Institute for Medical Sciences and Technology in Trivandrum and its forerunner, the Sree Chitra Tirunal Medical Centre. It would therefore seem presumptuous for it to claim any great influence on the growth of medical science in India. Nevertheless, the feeling that the emergence of the Institute marked a new departure in the history of medical science and technology in India is too strong to be passed over. It is not the hospital alone, as there are many equally good; nor is it the faculty, as there are others as well qualified; it is the convergence of medical science and technology in the organization of the Institute that has made it a unique institution of its kind.

Origin and evolution

The Institute inherited its name from Maharaja Sree Chitra Tirunal, erstwhile ruler of the State of Travancore. A year after the royal gift of a hospital building, the Government of Kerala under the leadership of C. Achutha Menon resolved to register the Sree Chitra Tirunal Medical Centre as a society for the promotion of higher specialities and research in medicine. The concern for excellence in research was so great that the Government of Kerala took the unusual step of placing the Centre under its department of science and technology and blazed a trail that was to shape its growth in subsequent years. To gain depth at the expense of breadth, an early decision was made to limit the services of the hospital to cardiology and neurology. These opened in 1976 and attracted patients whose number soon gave rise to pressure for the expansion of hospital services. This was hardly surprising because cardiac and neurologic care in the country was inadequate and the Institute offered free hospitalization to the poor and subsidized care for the middle-income groups. A new multi-storeyed block was added to accommodate the expansion in services which doubled within five years of their appearance.

The successful record in hospital services did not obscure the scientific objective of the Medical Centre, which was conceived as an institution of learning and research to which the hospital would provide clinical inputs. A field of endeavour that would embrace scientific interest, social relevance and industrial potential had to be identified. The choice fell on biomaterials and medical devices, which had failed to attract the attention of planners and national research organizations in spite of their relevance to patient care and large demand. A steadily growing market in the post-Second World War years had, in fact, created a multi-million dollar industry for medical devices abroad and a 'guesstimate' of India's imports had placed their annual price tag at 400–500 million rupees in the early seventies. As the first step, the Medical Centre initiated a project for the development of PVC and titanium for medical applications with financial support from the Department of Science and Technology. Apart from paving the way for the subsequent development of PVC bags for blood storage and the fabrication of a titanium housing for valvular prostheses, the DST project served to build a team of scientists and engineers and a favourable climate for intensifying the technologic effort. The acquisition of a new campus and the construction of a series of integrated laboratories quickly followed and produced a technologic counterpart for the hospital. The significance of the new experiment in integrating medical science and technology was recognized by the Government of India, who brought forward legislation to make the institution an 'institute of national importance'. The objectives of the Institute as defined in the Act were the development of biomedical engineering and technology, demonstration of high-standard patient care, and organization of integrated training programmes. The commencement of the Act in 1981 was a major milestone in the history of the Institute. Statistics for the period 1976–1989 demonstrate the rapid growth of the Institute (see figures and table).

If the staff strength rose dramatically from a double-digit figure to 500 during 1976–1979, its subsequent increase to 800 took a decade, a substantial part of the increase being claimed by the category of technical personnel such as nurses, technicians, radiographers and other paramedical staff (Figure 1). The rise in outpatient attendance, admissions, laboratory procedures and major operations matched the increase in personnel (Figure 2) and highlight the large demand for hospital services. What the statistics fail to disclose is the enormous goodwill that the Institute receives from the public thanks to its liberal policy on hospital services and concern for excellence in nursing. The figures on research grants, number of publications and patents (Table) are indicative of the state of health and progress of scientific research at the Institute. Given its modest size and tertiary structure, the performance statistics of the Institute are not unimpressive.

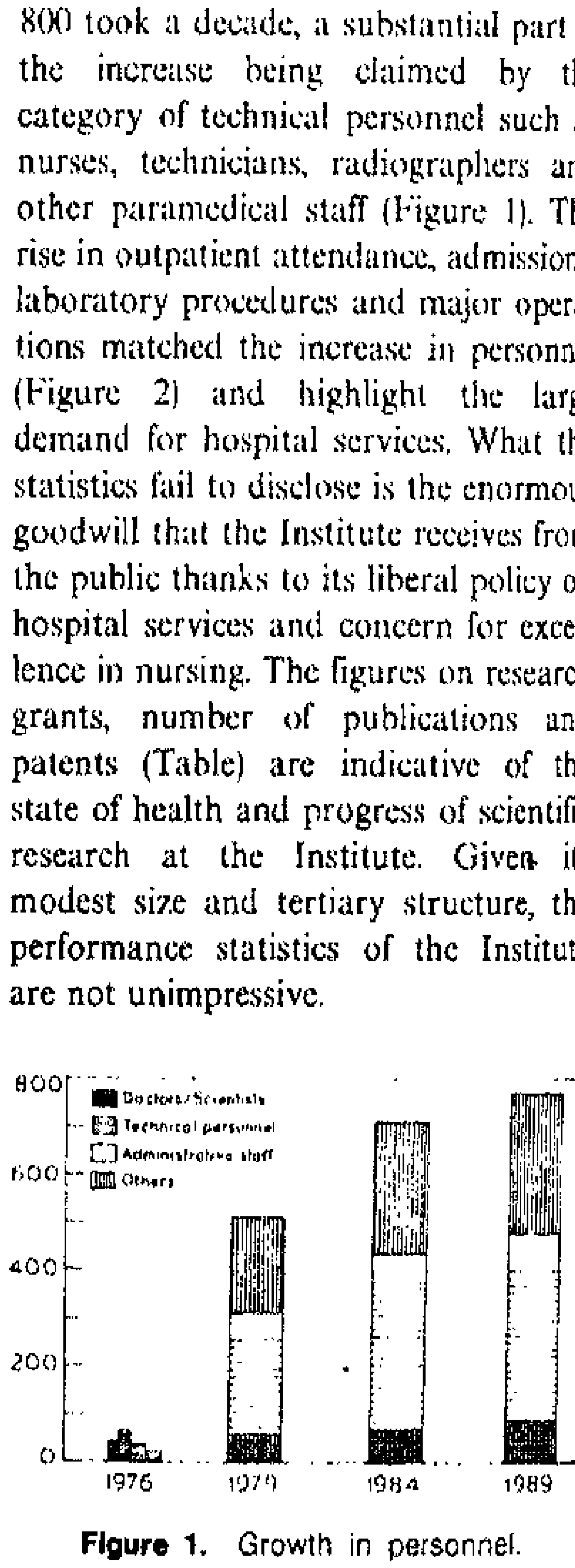


Figure 1. Growth in personnel.

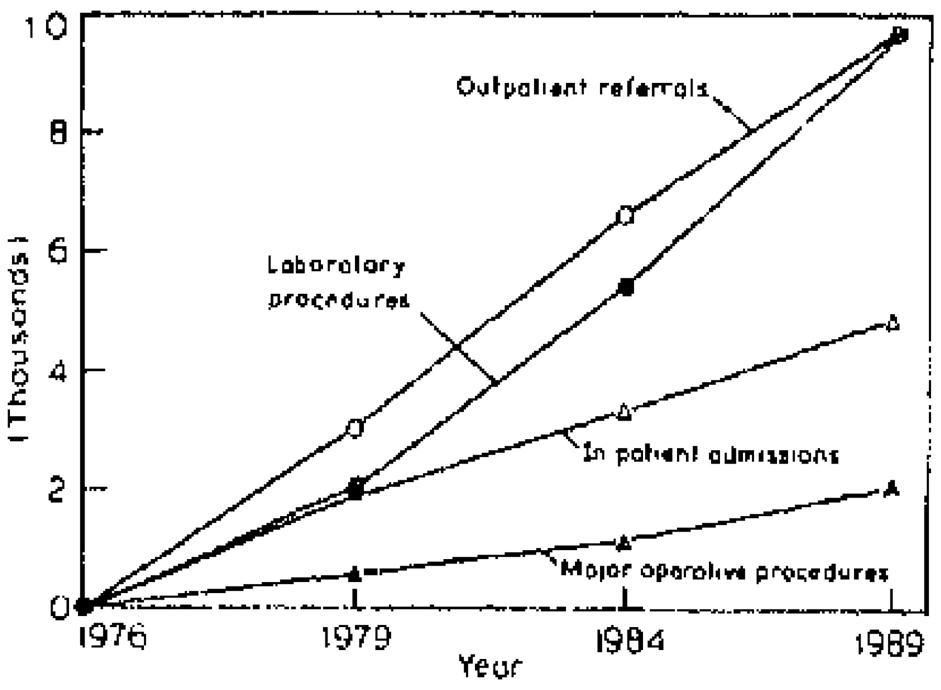


Figure 2. Expansion in hospital services.

Growth of research and development at SCTIMST

	1976	1979	1984	1989
1. Externally funded projects				
Number	0	0	8	18
Funding ('000s of rupees)	0	0	102.4	376.8
2. Number of patents				
Filed	0	0	2	7
Sealed	0	0	0	3
3. Number of publications	0	2	26	48

The Institute today

Hospital wing

The Institute has three campuses in Trivandrum, which house its hospital, technology wing and residential units. The hospital has 200 beds and serves as a tertiary referral centre for cardiovascular, thoracic and neurologic diseases. Staffed by highly qualified personnel, its departments have up-to-date facilities for diagnosis and treatment, including doppler echocardiography, cardiac catheterization with digital subtraction angiography, CT scan, intervention radiologic procedures, balloon and laser angioplasty, surgery for intracranial vascular lesions, and open heart surgery for congenital and acquired diseases of the heart. These services are offered free of charge to poor patients, who constitute over 50% of the total, with the result that the supply has fallen far short of demand. The cardiac and neurologic departments are fully supported in their programmes by sister departments such as anaesthesia, biochemistry, blood transfusion, microbiology, pathology and radiology. Apart from their direct responsibility in patient services, all these departments carry out clinical and experimental research of their own. The medical record system is well developed, with a computerized patient data base and established procedures for microfilming old charts.

Technology wing

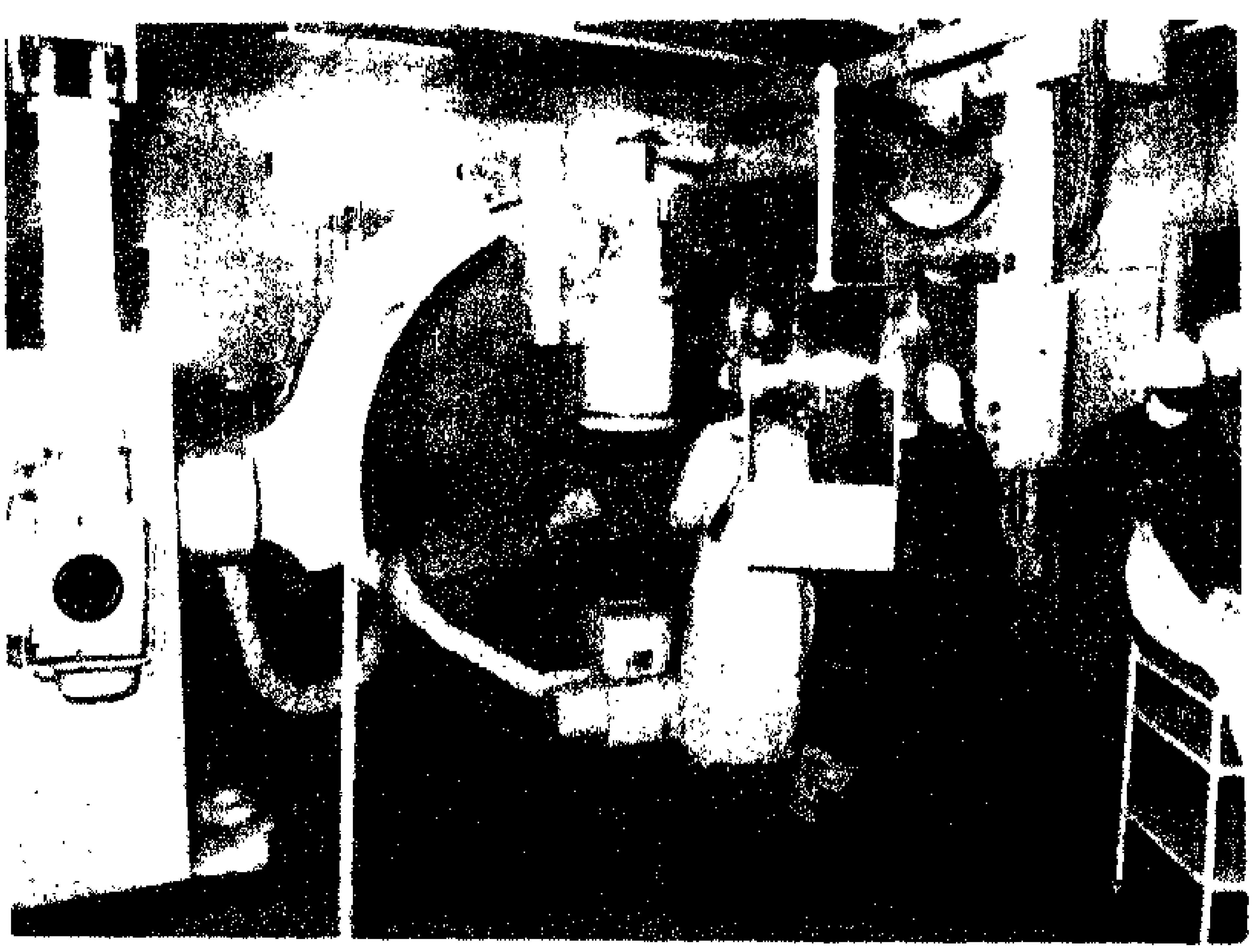
The technology wing is located at the Satelmond Palace Campus, 8 kilometres from the hospital. It consists of a series of laboratories for research and development in biomedicine and medical technology. They include units for the technical evaluation of materials, batch preparation of polymers, polymer chemistry, thrombosis research, polymer technology, biosurface studies, materials toxicology, biomaterials technology, pathophysiology and radiation sterilization (Panbit), and a tool room and vivarium. There are also Technoprove, a facility for evaluation of medical products, and a technology transfer unit. The hospital and technology wings have separate libraries, which subscribe to over 450 journals and maintain excellent collections of books in the areas of interest to the Institute. While the technology wing has its own faculty hostel for scientists, the hospital wing has nurses' hostels as well as a residential campus, which offers flats for the faculty and postgraduate students and dwelling units for other categories of staff.

Postgraduate courses

As an institute of national importance, the Institute has the status of a university and offers regular training programmes leading to the DM and MCh degrees in cardiac and neurologic disciplines, and PhD in biochemistry, microbiology and biomedical technology. The Institute also offers postdoctoral certificate courses in anaesthesia and radiology and a post-basic course in cardiovascular nursing. The courses attract so many applicants from across the country that the available seats are hardly twenty per cent of the number of applicants.

Medical technology and biomedical research

Over the years the research endeavour of the Institute has sought to develop medical products or processes on the one hand and investigate biomedical problems whose immediate applications are less obvious on the other. These efforts have received equal encouragement as the line of demarcation between applied research and basic research is ill-defined and misleading in the biomedical field. From the organizational



Cardiac catheterisation laboratory. State-of-the-art facilities including digital subtraction angiography for cardiac diagnosis, angioplasty and other procedures

Disposable blood bag. Among its merits, ability for component separation and avoidance of reuse rate high.

standpoint, the development of products or processes does call for a multidisciplinary approach whereas the investigation of 'basic problems' is often the work of a single group whose need for collaboration with other disciplines may be small. It is appropriate to discuss a series of examples to get a flavour of the ongoing effort at the Institute in medical technology and biomedical research.

Development of medical devices

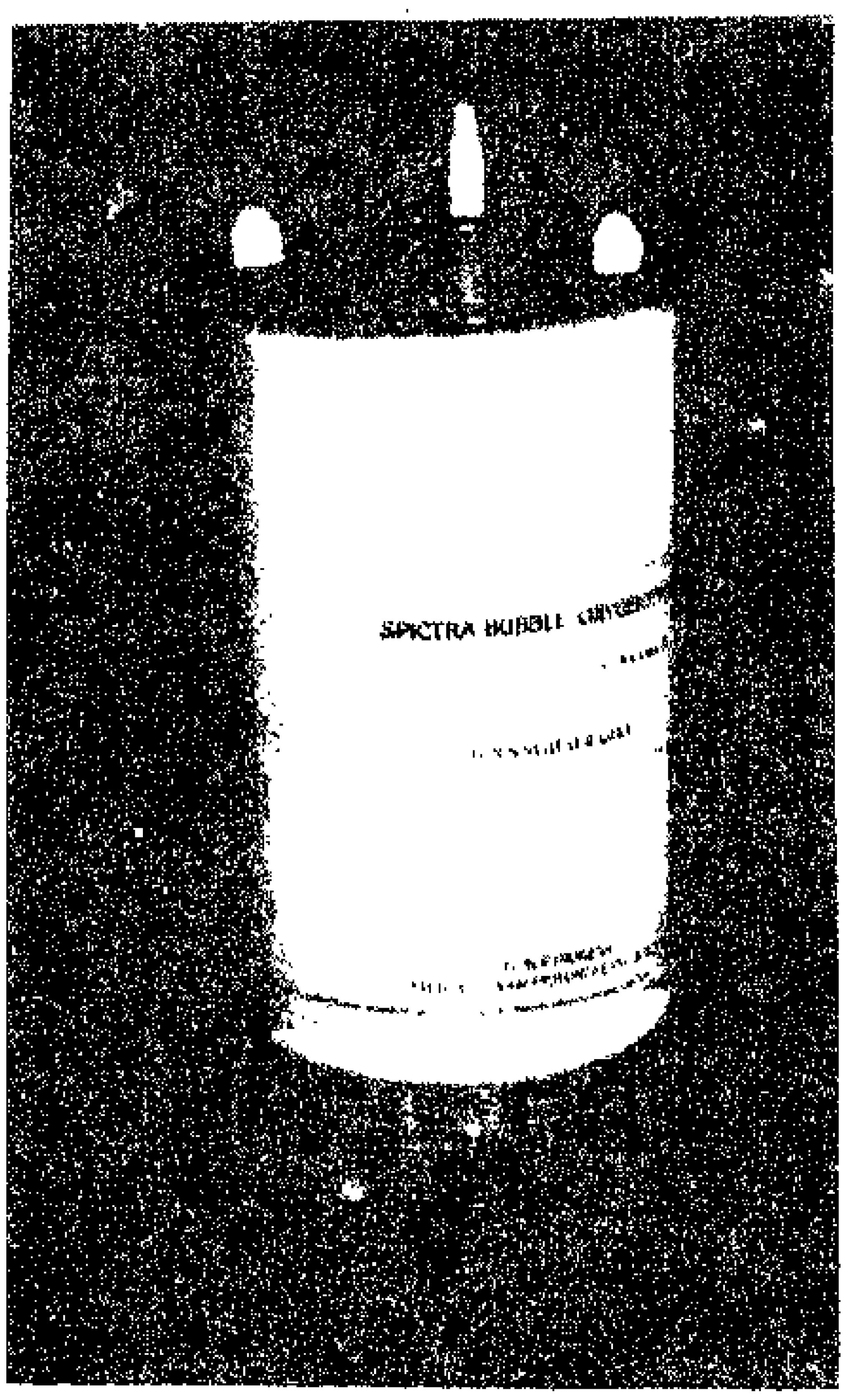
As blood bags for collection, storage and component separation of blood are indispensable for a transfusion service in the country, the Institute developed the technology for blood bags in conformity with international standards as the first essay in product development. Based on a PVC compound with negligible levels of leaching of phthalate, the blood bags are already being produced commercially by a joint-sector company. It is pertinent to note that blood bags are manufactured by no more than a handful of countries in the world. This was followed by the development of a blood oxygenator and a cardiotomy reservoir, two disposable devices used in open-heart surgery, currently imported. Industry-sponsored pilot production of these complex devices is now on and commercialization of production is expected at the conclusion of the current trials. Development of a stainless steel dental band, a tilting disc heart valve and a hydrocephalus shunt has advanced sufficiently for production to be expected within the next two years. The Institute estimates that the annual production of medical devices based on its technologies may be worth several tens of millions of rupees by the end of the Eighth Plan and that they may trigger the growth of a medical devices industry in the country. Without exception, the development of these technologies has involved the closest collaboration between the departments and divisions of the biomedical technology wing and the hospital.

Biomedical research

The variety and scope of the research effort in biomaterials and medical sciences offer a study in contrast to the product-oriented approach of medical technology. A major investigative programme, for example, is focused on prosthetic surfaces and their modification for biocompatibility. A variety of techniques have been employed to graft albumin, hydrogels, biomolecules like prostaglandin E_1, polyelectrolytes, urokinase complexes and indomethacin to foreign surfaces in an effort to improve the blood compatibility of the latter. These studies involve not only the development of new procedures for the immobilization of biomolecules and their characterization but also excursions into the experimental application of modified surfaces. The applications include small-diameter vascular graft, haemodialysis membranes and artificial skin. The aim of these wide-ranging studies is to deepen our understanding of biocompatibility and, ultimately, to tailor artificial substrates for living cells.

Another aspect of biomaterials research relates to the preparation and evaluation of hydrogel microspheres for application in embolotherapy, which has established itself in the management of haemorrhages, arterio-venous malformations and malignant tumours. In initial experiments, high-water-content microspheres were derived by a special process from cross-linked polymethylmethacrylate by alkaline hydrolysis. A procedure to prepare microspheres of desired size was also developed. The microspheres prepared in this manner not only successfully passed tests for biocompatibility and occlusive ability in an animal model but also offered a spin-off benefit as microcarriers for the culture and propagation of anchorage-dependent mammalian cells. More recently, many novel materials in the form of microspheres have been developed to provide radio-opaque materials, which are necessary for clinical embolotherapy. The cross-linked polymethylmethacrylate microspheres have in fact been cleared by the Institute's ethics committee for clinical trial.

Turning from the prosthetic to the biological end of the research spectrum, one may take note of the studies on platelet aggregation, which looms large in the field of coagulation. Making use of available information, a sequential shape change and interaction model of platelet aggregation kinetics was proposed and a rate equation derived on the basis of the model to provide a



Disposable blood oxygenator. With bubble chimney, defoaming chamber and heat exchanger, serves as the 'lung' during heart-lung bypass or open-heart operations.

rationale for interpreting platelet aggregation kinetics. A spectrophotometric method was also developed to follow single-platelet recruitment into aggregates. Using these tools the aggregation kinetics was found, except in the case of ADP-induced aggregation, to follow a positively cooperative pattern modifiable by platelet antagonists. These investigations led to the discovery of a platelet haemoprotein that could apparently function as receptor for platelet activating factor, PGH_2 and several unsaturated fatty acids, and mediate in the effect of agents such as Ca^{2+}, Cd^{2+} and diltiazem. The implications of these studies for antiplatelet therapeutics are obvious.

Human myocardial cells in culture. Test of a hypothesis for aetiology of endomyocardial fibrosis.

From platelets, one moves on to the study of cell-cell communication and the interaction of sugar-binding proteins (lectins) with their cell-surface glycoconjugate receptors. The isolation and characterisation of a new high-molecular-weight galactose-binding lectin from bovine heart muscle was followed by studies on lectin receptors and lectin-receptor interaction in mammalian brain in which three different lectin-binding glycoproteins were shown. Anti-galactoside antibody (anti-Gal), present only in human and Old World monkey sera and capable of preventing tumour cells from anchoring to lung basement membrane, was purified to homogeneity. Efforts to isolate plant galactose-binding lectins resulted in the purification and characterization of three lectins. Investigations on several aspects of lectins form a major part of biochemical research at the Institute.

In the domain of medicine, it was inevitable that endomyocardial fibrosis should claim attention, because of its prevalence in Kerala. Studies on the disease, which is a form of cardiomyopathy, became the nucleus for the advanced centre for cardiomyopathies sponsored by the Indian Council of Medical Research at the Institute. Reported from Kerala more than two decades ago and noted in Africa earlier, its causation had remained an enigma wrapped in an eosinophilic hypothesis. Analytical studies carried out in collaboration with the Bhabha Atomic Research Centre, Bombay, however showed that the endomyocardial tissues of patients contained significantly higher concentrations of cerium and thorium, which are constituents of the monazite soil of Kerala, and lower levels of magnesium than control samples. These findings suggested a geochemical, rather than an eosinophilic, basis for the disease and placed its aetiopathogenesis in a nontraditional context. The geochemical hypothesis is currently under validation by experimental production of the disease in animals and by further studies of magnesium–cerium interaction at the cellular level in a human myocardial cell culture system.

In summary, the research programmes of the Institute are varied, exciting and never far from the human situation.

Conclusion

There is a general impression that Indian institutions of learning follow a characteristic pattern of evolution during the first forty to fifty years, when they pass, sequentially, through phases of rapid growth, plateau, decline and bureaucratic ossification. Whether one subscribes to this theory or not, there is little doubt that sustaining institutional excellence is a greater challenge than creating it, particularly in India. Young as it is, Sree Chitra Tirunal Institute can hope to preserve excellence and escape the usual fate only to the extent that it generates ideas that respond to the changing demands of medicine and health-care technology in the country. Herein lies the challenge as well as an opportunity for the Institute.

Demographers estimate that India's population may stabilize around 1.5 billion by the middle of the next century. The greatest challenge, if not nightmare, for the medical planner is the provision of adequate hospital services to the growing millions, who will refuse to settle for conditions of wretchedness in hospitals in the years to come. Nor can the medical planner ignore the steady advances in medicine worldwide, which will escalate the demand for similar practices nearer home and add to the problem of inadequacies in our hospital services. Unfortunately, as our hospital practice survives on the import of instruments, medical devices, biotechnology products and even ideas, high-quality patient care cannot but remain out of reach for the bulk of our population. In confronting the hardest problem of expanding high-quality care, one may, however, be closest to its answer, which technology alone can supply. As the last sands of the twentieth century run out, Sree Chitra Tirunal Institute may have its finest hour in giving a technological uplift to the hospital services of the nation and increasing their accessibility. It can render no better service and bequeath no greater heritage to the next hundred years of medicine in this country. Nor can there be a stronger vindication of the unified vision that animates its endeavour.

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